"The BCoS Cognitive Profile Screen: Utility and Predictive Value for Stroke."

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Abstract

Objective: We examined the utility of the Birmingham Cognitive Screen (BCoS) in discriminating cognitive profiles and recovery of function across stroke survivors. BCoS was designed for stroke-specific problems across 5 cognitive domains: (a) controlled and spatial attention, (b) language, (c) memory, (d) number processing, and (e) praxis. Method: On the basis of specific inclusion criteria, this cross-section observational study analyzed cognitive profiles of 657 subacute stroke patients, 331 of them reassessed at 9 months. Impairments on 32 measures were evaluated by comparison with 100 matched healthy controls. Measures of affect, apathy, and activities of daily living were also taken. Between-subjects group comparisons of mean performance scores and impairment rates and within-subject examination of impairment rates over time were conducted. Logistic regressions and general linear modeling were used for multivariate analysis of domain-level effects on outcomes. Results: Individua...

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THE BCOS COGNITIVE PROFILE SCREEN: UTILITY AND PREDICTIVE VALUE FOR STROKE

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ABSTRACT

Objective: To review the predictive and discriminative value of cognitive profile from a screen (BCoS) for the long term functional and cognitive outcomes across groups of different stroke history and lesion sides. The screen assessed abilities across and within 5 domains: controlled and spatial attention, language, memory, number processing and praxis. *Methods:* Based on specific inclusion criteria, this cross-section observational study analysed cognitive profiles of 657 sub-acute stroke patients, 331 of them reassessed at 9 months. Impairment on 32 measures were assessed by comparison to 100 matched healthy controls. Measures of affect, motivation, and activities of daily living were also taken. Between-subject group comparisons of mean performance scores and impairment rates, as well as within-subject examination of impairment rates over time were conducted. Logistic regressions and general linear modelling were used to conduct multivariate analysis of domain level effects on outcomes. *Results:* Functional outcome at 9 months was reliably predicted by domain-level deficits in controlled and spatial attention and praxis, over and above initial dependency, concurrent levels of affect and motivation. Predictions were increased when problems in controlled attention were included along with other domain measures. There was better recovery for patients after their first stroke than after multiple strokes, and better recovery for right hemisphere lesioned patients in praxis tasks which was not due to reductions in neglect. The sub-domain patterns of recovery across stroke/lesion types were also revealed. *Conclusion*: The results highlight the utility of developing a cognitive profile for patients for predicting outcome and to inform rehabilitation.

INTRODUCTION

Cognitive deficits are prevalence at the acute stage of stroke[1]. They interfere with the potential benefits of rehabilitation, impact on recovery[2-13] and associate with a poorer quality of life[14-16] and depression[13, 17]. Neuropsychological assessments have typically divided cognitive functions into several domains (e.g., attention, language, memory[18]) as supported by evidence of clustered patterns of brain activity[19]. The co-occurrence of impairments in two or more domain functions, such as impaired executive functions or sustained attention alongside language impairments/neglect, may adversely affects the rehabilitation outcome of the primary function i.e. in language[20] or visual attention[21, 22]. Therefore, assessment needs to cover the primary symptoms as well as the contributing, co-occurring impairments. Whilst early cognitive screening for stroke is well recognised[23], the existing screening tools (e.g. the MMSE[24], the MoCA[25], the ACE-R[26]) were not stroke specific. There were often no evaluation the common post stroke deficits of spatial neglect[27] or apraxia[28]; nor procedures to minimise contamination of effects of aphasia or neglect on performance of non-language/visuospatial tasks (e.g. memory tests). BCoS[29] aimed to address these as a time efficient, inclusive and comprehensive assessment for stroke. BCoS's principles and designs, validity and reliability are published elsewhere[28-30]. The current paper reports data from a large-scale trial assessing the utility and functional predictive value of BCoS across a population of sub-acute stroke patients. We first examined the behavioural profiles and patterns of recovery of the patients by their stroke history (first stroke or repeated stroke), and whether the stroke affected the left or right hemisphere[31]. We then examined the utility of

BCoS for predicting functional outcome at 9 months, controlling for affect and initial dependency level.

METHODS Participants. Stroke survivors were recruited between Nov 2006 and Jan 2011 from 12 hospitals in the West Midlands as a part of a UK cognitive screen trial (the Birmingham University Cognitive Screen, www.bucs.bham.ac.uk). Stroke survivors were recruited if medically stable, within 3-months of their latest stroke and able to give informed consent. Diagnosis of a stroke was based on the assessment by the clinical team. Exclusion criteria were 1) insufficient understanding of English; 2) inability to concentrate for 35 minutes; 3) premorbid conditions affecting cognition (e.g., dementia).

Lesion information from hospital-based CT or MRI scans (where available) was obtained. Patients were excluded if there was no observable focal damage or if image quality was poor. About 50% of the participants took part in a 9-months follow up assessment (see figure e-1 for the flow chart of the patient cohort at baseline and follow-up). Patients who completed fewer than 15/22 tasks were excluded (10%), to enable us to have relatively complete datasets for each patient. The most common reasons given for task incompletion were 1) fatigue, 2) a lack of time. For the analyses related to the lesion side, only patients with observable unilateral lesion were included. Informed consent was obtained according to the approved ethics protocols of the UK National Research Ethics Committee. Data were collected by examiners (psychologists, occupational therapists or stroke researchers) trained and supported by the University team under the supervision of the chief investigator (GWH).

Cognitive screen measures. BCoS assesses five cognitive domains: attention and executive function, language, memory, number and praxis. Finer-grained distinctions can also be drawn within some of the domains including between (i) spatial attention (neglect, extinction) and attentional control (executive functions, sustained attention), (ii) spoken and written language, (iii) immediate and delayed memory, and (iv) apraxia and constructional apraxia. Further descriptions of the tests are provided elsewhere[29] and at www.cognitionmatters.org.uk. There are 32 different sub-measures derived from 22 tasks (see table e-1 for brief descriptions of the 22 BCoS tasks). Age-group (50-64, 65-74, 75 or above) specific cut offs (at 5th percentile) for each test were established from a hundred healthy controls stratified following the 2001 UK population census age x sex x education level distribution.

Affective and functional/dependency measures. At the initial assessment, Affect was measured by the Hospital Anxiety and Depression scale[32] (HADS) and dependency level was measured by the Barthel index[33]. At 9 months follow-up, the above were repeated along with the Apathy Evaluation scale[34] (AES) for motivation and the Nottingham Extended ADL scale[35] (NEADL) for participation in community ADL.

Statistical analysis. For the comparison of demographic and background details between sub-groups of interest, two tailed Mann-Whitney U tests were used for continuous non-normally distributed variables, T tests were used to compare continuous data and, chi-square was used to compare categorical data. For the comparisons of cognitive profiles at the cognitive domain level, MANOVAs were performed on all the scores of the subtasks that were part of the same cognitive

domain. Subsequent individual task level analyses used Mann-Whitney U tests for raw scores and chi-square for diagnosis category (unimpaired versus impaired). NcNemar tests were used to compare rates of impairment on each task individually at the initial and follow-up assessments. Bonferroni corrections were made to all multiple comparisons. Linear regressions were used to model effects on functional outcomes while controlling for other confounding factors and GLM was used to conduct multivariate analysis of domain level effects on outcomes.

Results

657 participants were included in the analyses. 455 (69%) were survivors of first stroke and 202 (31%) had had a previous stroke. Table 1 shows the demographic and health measures details of the participants, comparing across groupings of interest. We assessed whether stroke history (first or repeated stroke) and unilateral lesion side (left hemisphere or right hemisphere) affected cognitive ability and recovery (BCoS performance) after stroke (Part 1). We then evaluated whether longer-term functional outcome could be predicted by cognitive performance at sub-acute stage (Part 2), and whether there were gains from examining co-occurring deficits (Part 3).

Part 1: Stroke factors linked to cognitive outcomes.

First vs. repeated stroke effects. There was no difference in age, gender and education across patients with their first or a repeated stroke. Patients who had a first stroke were tested later than those who had a repeated stroke (mean difference = 6 days, $p<0.001$). Numerically, there was a trend for higher levels of depression in

repeated compared to first stroke patients but this did not reach the corrected level of significance. No other significant group difference was found.

Overall, the cognitive performance of the first and repeat stroke groups was very similar at baseline. Both groups completed an equal number of BCoS tasks (Table 2) and there were no group differences at either the cognitive domain level (all $p>0.01$, i.e. above the corrected level of significance 0.008, Table 2) or the task level (raw scores all $p>0.002$, Table 2; for the proportion of patients impaired: all $p>0.002$, Table 3).

Significant improvement (based on a reduction in the number of patients diagnosed as impaired) (Table 3) at follow-up was more frequent in the first stroke group (on average improving on 15/32 of the measures) compared to the repeated stroke group (improvements on only 4/32 measures; $\chi^2=9.06$, $p=0.003$). This differential improvement did not reflect underlying contrasts in age, gender, education and initial Barthel score, none of which differed. Patients with multiple strokes tended to be more depressed, which may have reduced their motivation to engage in rehabilitation. However we found no differences in the extent of task recovery between depressed and non-depressed patients with multiple strokes ($t(86)=-0.92$, $p=0.362$). The data also revealed instances of persistent deficits across both groups for spatial neglect (cancellation task accuracy and asymmetry) and verbal memory (immediate and delayed verbal recall and recognition measures). Within the praxis domain, gesture production and recognition deficits were more persistent than other impairments (though note the relatively lower initial impairment rates for gesture production and recognition).

Left vs. right unilateral lesion effects in first stroke patients.

Grouping by unilateral brain lesion side revealed no differences in the demographic details, the initial functional performance and level of affect (anxiety, depression) across the groups (Table 1).

Overall the LHD group had more cognitive impairments than the RHD group, completing fewer BCoS tasks ($p<0.000$) and showing a significantly worse performance in all cognitive domains with the exception of spatial attention (Table 2). In the spatial attention domain, the RHD patients performed more poorly than the LHD individuals on the cancellation task (overall scores and lateralized error scores) as well as on the left visual and tactile extinction tasks (all $p<=0.001$); individuals with LHD were more impaired in the right tactile extinction task ($p<0.001$). Lesion side was also significant when comparisons were made using rates of impairment (all $p>0.05$, except sentence reading $p>0.002$)

The LHD and RHD groups showed comparable extents of recovery (Table 3) (significant reduction of impairment in 4/32 measures for LHD and 6/32 measures for RHD patients). However, the LHD and RHD groups did differ in which specific tasks/domains improved (Table 3). Some of these differential patterns of recovery can be explained by the higher initial rates of impairment in some tasks leading to a higher probability of performance improvement (e.g. left visual extinction for RHD vs. LHD patients). However, this was not the case for the sentence construction task, the rule finding and switching task and the MOT task, where in each instance both groups started with similar rates of impairment but only the RHD group showed

significant recovery; also the RHD group was less impaired initially at imitation but showed greater improvement.

Part 2: Cognitive predictors of functional recovery in first stroke patients

There was a trend for followed-up patients to have more years in education (mean difference 0.6, p=0.022) and to be more depressed than those not followed up (p=0.017)(not significant corrected)(Table 1). No other significant differences were found on the demographic, initial functional and affective characteristics of the groups. Concerning the initial cognitive profile, no significant difference was found between the follow-up and non-follow-up groups (table e-2).

Using as predictors the overall cognitive impairment at initial assessment (i.e. the proportion of tasks impaired), and controlling for the initial Barthel, follow-up HADS scores and follow-up apathy scores, the proportion of BCoS tasks impaired was an significant predicting factor for the NEADL score (B(SE)=-3.47(1.22), beta=-0.173, p=0.005) (Table 4).

We then used as a predictor a domain level diagnosis: “impaired” when performance on any one task was impaired, or not completed within a domain, versus “not impaired” when performance was unimpaired on all tasks within a domain (Table 5). Three domains were significant predictors of the NEADL score: spatial attention (Lambda=0.920, p=0.001), controlled attention (Lambda=0.959, p=0.036) and praxis (Lambda=0.919, p=0.001). No predictors were found for the follow up Barthel scores.

Part 3: The importance of co-occurring deficits

To examine the impact of co-occurring deficits in controlled and spatial attention, we assessed performance within the domains that predicted the NEADL (namely spatial attention, controlled attention and praxis; see Table 5) and evaluated whether the variance accounted for in the NEADL increased for the praxis domain when the attention domains (spatial and controlled) were taken into account. Variance in the NEADL at 9 months was better accounted for when the attention domains were considered (R^2 increased by 7.5%, $p<0.001$ to 55.5%), consistent with cognitive profiling of attention adding to predictions from single deficits alone. In addition, performance in picture naming and sentence construction at 9 months were better predicted by taking the initial auditory attention score (including verbal working memory) into account along with initial picture naming (β=0.023, 95% CI 0.006, 0.04, p=0.01) and sentence construction (β=0.013, 95% CI 0.004, 0.022, p=0.005) respectively. It is more the case for predicting cancellation accuracy when taking the initial executive function score (β=0.214, 95% CI 0.049, 0.378, p=0.011) along with the initial cancellation task; while reduction of cancellation asymmetry was better explained by including the initial auditory attention score (β=0.039, 95% CI 0.007, 0.07, p=0.018) alongside the first measure of cancellation asymmetry. The presence of poor working memory, sustained attention, and response inhibition (measured in the auditory attention task) and poor executive function, led to better prediction of longer-term language and spatial attention problems.

Discussion

The BCoS provides a cognitive screen for stroke that is relatively time efficient (completed in around 1 hour) and inclusive (90% of patients tested at a sub-acute

stage were able to complete >75% of tests designed to be ‘aphasia and neglect friendly’). It provides a ‘cognitive profile’ for patients covering language, memory, number processing, praxis and spatial and controlled attention. Our results indicate that (i) there were differential effects of whether patients have suffered their first stroke or had a repeat stroke, (ii) and whether the stroke affected the left or right hemisphere, while (iii) overall cognitive performance predicted outcome at 9 months, taking into account the initial functional performance score (the Barthel index) and affective characteristics (depression, anxiety and apathy measures). We consider each point in turn.

First vs. repeat stroke

There were no reliable differences in overall cognitive performance in patients who suffered their first stroke relative to those who had a prior history of stroke, and for all patients the spatial attention and verbal memory problems were most persistent (showing fewest gains in terms of the patients who were impaired at follow-up compared with the initial test). There were interesting differences however in the numbers of patients who did and did not show recovery. In particular, more first-stroke patients went from an impaired to a non-impaired category relative to patients with repeat strokes. This was not due to initial differences in task performance, overall physical function (Barthel index) or age (the groups did not differ on any of these variables). There was also no difference in the initial time of testing between patients who did and those who did not show recovery ($t(329)=0.485$, $p=0.612$) and nor did the recovering and the non-recovering patients differ in their initial affect (Anxiety, $t(311)=-0.967$, Depression, $t(311)=-0.293$). This last result means that the

lack of recovery after repeat stroke is unlikely to reflect purely motivational factors. One alternative account is that neural plasticity decreases after there has been an earlier neurological insult. This speculative proposal requires further verification in experimental models, however it does fit with the relatively high incidence of dementia that can arise after stroke[8].

Left vs. right hemisphere damage.

Patients with unilateral left hemisphere damage overall fared worse than patients with a unilateral right hemisphere lesion. At a domain level, the LHD patients were worse on the language, memory, number and praxis tests, with the opposite pattern present only for spatial attention. It can be argued that many of these tests required language and/or communication abilities (language, praxis and number tests), and this was also the case for memory given that the BCoS features a verbal LTM task (though forced-choice tests are used to assess recognition memory). Indeed many of the tests not showing a reliable contrast between LHD and RHD patients (rule finding and switching task, multiple object use and figure copy) were putatively less language demanding. The RHD patients were impaired across a range of spatial attention tasks testing neglect and extinction, consistent with the right hemisphere playing a dominant role in controlling human attention[36].

Interestingly, though the LHD and RHD patients were both impaired on the rule finding and shifting task and the multiple object use task, only the RHD patients showed significant recovery of function. The recovery of the patients on the rule finding and shifting task correlated with recovery in neglect ($\chi^2(1)=7.297$, $p=0.007$) but this was not the case for the multiple object use task ($\chi^2(1)=0.195$, $p=0.659$). If

recovery based on reductions in neglect is implausible for the multiple object use task, then an alternative possibility for is that, for this task, the presence of relatively spared language abilities in the RHD group enabled them to improve by using a verbal record of the actions carried out[37]. One result consistent with this is that the patients who improved on the rule and multiple object tasks tended to have better language functions than those who did not improve (t(71)=3.320, p=0.002 and t(63)=2.516, p=0017, for picture naming and sentence construction).

Predicting functional outcome

Previous studies have indicated that functional outcomes can be accounted for by measures of cognitive deficits[13]. Similar to these studies, we demonstrated that an easy-to-derive index from BCoS, the number of sub-tests where an impairment was detected, predicted our primary outcome measure of function at 9 months – scores on the NEADL. Predictions from the BCoS occurred over and above effects due neuropsychiatric symptoms (depression, anxiety and apathy) and both initial and longer-term motor impairment (Barthel index). The domains that were most effective for capturing the NEADL were spatial and controlled attention and praxis (Table 5). It is interesting that few other general screens for cognitive problems (e.g., the MOCA; the ACE-R) provide specific measures of spatial attention and praxis and none (to our knowledge) capture the conjoint effects of working memory, selective and sustained attention as here. The results point to the important of measuring the problems of patients in these domains for predicting their longer-term outcome.

The finding that deficits in controlled attention predict functional outcome is also of interest because models of cognition suppose that aspects of the controlled attention

tests interact with other processes to support different cognitive abilities. For example, working memory and sustained attention are important to support processes ranging from scanning the environment through to sentence comprehension and production[21, 38], while attentional suppression (e.g., affecting the ability to ignore irrelevant stimuli) may facilitate multiple tasks where distractors are present [39]. Interestingly we found that we were able to account for more variance in our functional outcome measure (the NEADL) and language and spatial impairments at 9 months when deficits in controlled attention were modelled along with initial deficits in spatial attention and praxis. This points to the utility of using a battery such as the BCoS, which derives a cognitive profile including measures of working memory, sustained attention and executive function. This, when coupled with the inclusivity of the battery (e.g., for aphasic and neglect patients), the sensitivity to important clinical impairments after stroke (e.g., apraxia[28] and neglect[30]) and its easy clinical reporting scheme, as illustrated by Bisiker and Bickerton's clinical example[40] affirm BCoS's potential benefit to stroke care.

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Table 1 Demographic and health measures of patients compared by stroke history, lesion side and followed-up status

						first stroke only					first stroke only				
	First stroke		Repeated stroke			LHD		RHD			FU		no FU		
		SD		SD	p[a]		SD		SD	p[a]		SD		SD	p[a]
N	455		202			152		181			240		215		
Age	69.31	14.34	71.38	12.60	NS	69.34	13.93	69.42	14.51	NS	70.00	13.26	68.53	15.44	NS
Gender (% female)	44.80		39.6		NS	46.70		42.00		NS	45.00		44.70		NS
Year of education	11.52	2.76	11.19	2.76	NS	11.55	2.79	11.66	2.83	NS	11.80	2.91	11.20	2.55	0.022
Time post current stroke	26.65	22.36	20.44	17.29	0.000**	28.52	23.96	25.89	21.72	NS	26.83	20.95	26.46	23.88	NS
Initial Barthel	13.01	5.76	13.34	5.43	NS	12.72	5.92	12.63	5.96	NS	12.60	5.70	13.47	5.80	NS
Initial HADS anxiety	6.22	4.50	6.70	4.98	NS	6.11	4.44	6.08	4.62	NS	6.61	4.59	5.77	4.36	NS
Initial HADS depression	5.71	4.05	6.66	4.29	0.009	5.64	4.24	5.64	4.02	NS	6.15	4.13	5.20	3.90	0.017
For followed up subgroup															
Proportion followed up %	52.70		45.00		NS	50.00		59.70		NS					
Followed up Barthel	17.00	4.11	17.19	3.84	NS	17.39	3.58	16.19	4.78	NS					
NEADL	12.79	6.48	12.90	6.56	NS	12.36	7.01	12.29	6.51	NS					
FU HADS anxiety	5.58	4.38	6.21	4.85	NS	4.86	3.55	6.08	4.56	0.050					
FU HADS depression	5.43	3.71	6.69	4.39	0.018	4.96	3.78	5.75	3.72	NS					
Apathy evaluation score	31.91	9.99	34.36	10.10	NS	31.46	8.64	33.00	10.89	NS					

[a]T-test significance NS at= 0.05 level

**statistical significance with Bonferroni correction, p at 0.05/7=0.007

Table 2 Baseline cognitive profile of patients grouped by stroke history and lesion side

			Comparing first and repeated stroke					**Comparing LHD vs RHD (first stroke only)**				
Domain	**Measure**	**Max.**	**first**		**repeated**			**LHD**		**RHD**		
		score	**Mean**	**SD**	**Mean**	**SD**	**p[a]**	**Mean**	**SD**	**Mean**	**SD**	**p[a]**
No. tasks completed (out of 22)			21.03	1.76	20.96	1.71	NS	20.58	2.23	**21.35**	1.29	0.000**
Attention							**NS**					**0.000****
Attention	cancellation accuracy	50	39.94	13.14	39.55	13.45	NS	**43.27[b]**	9.83	36.20	14.94	0.000**
- Spatial	*page based asymmetry (abs)[c,]*	20	2.69	3.92	2.99	4.89	NS	**1.45**	1.89	3.89	4.82	0.000**
	object based asymmetry (abs)[c,]	20	1.47	3.48	2.02	5.31	NS	**0.81**	2.68	2.38	4.46	0.001**
	left visual bilateral	8	6.95	2.45	6.95	2.49	NS	**7.85**	0.65	5.97	3.16	0.000**
	left tactile bilateral	8	6.95	2.39	7.08	2.18	NS	**7.78**	1.00	6.01	3.11	0.000**
	right visual bilateral	8	7.62	1.49	7.47	1.73	NS	7.28	2.12	7.83	0.94	0.005
	right tactile bilateral	8	7.63	1.36	7.49	1.57	NS	7.09	2.16	**7.92**	0.43	0.000**
Attention	rule finding and switching	18	7.15	5.86	6.47	5.29	NS	7.23	5.79	7.30	5.75	NS
- Controlled	auditory attention accuracy	54	43.64	13.90	43.64	12.42	NS	37.89	16.24	**46.91**	11.20	0.000**
	practice required	3	1.44	0.75	1.52	0.77	NS	1.63	0.84	1.35	0.70	0.004
	word recalled	3	2.62	0.67	2.55	0.75	NS	2.48	0.75	2.70	0.59	0.011
Language							**NS**					**0.000****
	picture naming	14	11.32	2.67	11.30	2.46	NS	10.71	3.14	11.69	2.21	0.003
	sentence construction	8	7.06	1.73	7.10	1.60	NS	6.95	1.96	7.18	1.41	NS
	sentence reading (accuracy)	42	38.88	7.33	37.67	8.31	NS	38.07	8.56	39.04	7.08	NS
	nonword reading (accuracy)	6	4.58	1.83	4.59	1.91	NS	3.86	2.15	**4.92**	1.53	0.000**
	word writing	5	3.24	1.63	3.19	1.73	NS	2.80	1.77	**3.48**	1.53	0.001**
	comprehension	3	2.91	0.30	2.88	0.35	NS	2.87	0.36	2.93	0.26	NS

Memory							**NS**					**0.000****
	personal info	8	7.66	0.99	7.59	1.00	NS	7.35	1.42	**7.83**	0.52	0.000**
	time and space	6	5.62	0.79	5.55	0.84	NS	5.61	0.94	5.62	0.69	NS
	immed free recall	15	6.52	3.23	6.16	3.13	NS	5.72	3.17	**7.18**	3.15	0.000**
	immed recognition	15	12.26	2.85	11.92	3.04	NS	11.73	3.27	12.71	2.35	0.004
	delayed free recall	15	7.32	4.16	6.45	4.03	0.021	6.18	4.37	**7.99**	3.80	0.000**
	delayed recognition	15	12.96	2.84	12.53	2.92	NS	12.27	3.47	**13.34**	2.34	0.001**
	task recognition	10	8.64	1.89	8.33	1.99	NS	8.31	1.97	8.83	1.60	0.016
Number							**NS**					**0.000****
	number reading	9	7.60	2.51	7.35	2.76	NS	6.70	3.29	**8.09**	1.83	0.000**
	number writing	5	3.89	1.63	3.68	1.74	NS	3.39	1.93	**4.25**	1.20	0.000**
	calculation	4	2.54	1.39	2.37	1.45	NS	2.25	1.50	2.71	1.27	0.004
Praxis							**0.017**					**0.000****
	multiple object use	12	10.20	3.28	10.15	3.42	NS	9.82	3.78	10.15	3.08	NS
	gesture production	12	10.43	2.57	10.55	2.44	NS	9.26	3.44	**11.09**	1.43	0.000**
	gesture recognition	6	5.02	1.19	4.90	1.21	NS	4.65	1.44	**5.22**	0.98	0.000**
	gesture imitation	12	9.44	2.74	9.05	3.09	NS	8.86	3.11	9.74	2.47	0.005
	figure copy	47	34.86	11.19	32.06	12.79	0.007	35.22	11.23	33.79	11.54	NS

**significant at 0.002 level. Abbreviations: LHD = left brain damaged; RHD = right hemisphere damaged; SD = standard deviation. [a]Statistical significance at domain level (in bold) refers to the multivariate statistics; at task level, it refers to between subject effects, NS at 0.05 level. [b]Figure in bold and underlined are the scores showing significant better performance (i.e. higher scores, except for the cancellation asymmetry scores and the auditory attention number of practice required (task names in italic, these are error based scores, the lower the scores, the better the performance)). [c]Page based asymmetry score for the cancellation task indicates extent of egocentric neglect, object based asymmetry score indicates allocentric neglect[30].

Table 3 Comparing percentage impairments across assessments in each measure between groups of different stroke history and different lesion sides

-		**First Stroke**			**Repeated Stroke**			**LHD**			**RHD**		
N		240			91			76			108		
Domain	**Measure**	**initial**	**FU**	**p[a]**	**initial**	**FU**	**p[a]**	**initial**	**FU**	**p[a]**	**initial**	**FU**	**p[a]**
Attention	cancellation accuracy	32.80	27.50	NS	31.6	20.3	0.035	19.70	21.20	NS	44.10	36.60	NS
- Spatial	page based asymmetry (abs)	26.50	18.60	0.029	27.8	21.5	NS	13.60	15.20	NS	38.70	25.80	0.043
	object based asymmetry (abs)	24.90	15.60	0.004	17.7	12.7	NS	15.20	6.10	NS	35.10	24.50	NS
	left visual bilateral	20.20	14.20	0.016	18.2	10.2	NS	5.50	2.70	NS	33.60	21.50	0.001**
	left tactile bilateral	19.50	13.00	0.003	15.6	12.2	NS	4.20	2.80	NS	32.10	22.60	0.013
	right visual bilateral	13.70	8.20	0.024	10.2	12.5	NS	19.20	9.60	0.039	7.50	4.70	NS
	right tactile bilateral	13.00	5.20	0.001**	12.2	6.7	NS	26.80	9.90	0.004	5.70	1.90	NS
Attention	rule finding and switching	41.00	24.80	0.000**	41.7	32.1	NS	37.70	26.10	NS	38.20	21.60	0.002**
- Controlled	auditory attention accuracy	41.50	28.60	0.000**	51.2	32.6	0.005	57.40	32.40	0.000**	32.40	24.80	NS
	practice required	25.90	21.40	NS	37.2	16.3	0.001**	35.30	32.40	NS	20.00	16.20	NS
	word recalled	22.00	8.10	0.000**	22.4	15.3	NS	30.90	11.80	0.004	19.00	6.70	0.002**
Language	picture naming	25.70	16.50	0.000**	23.1	14.3	NS	41.90	24.30	0.001**	13.90	12.00	NS
	sentence construction	27.80	9.70	0.000**	25	15.9	NS	26.20	12.30	0.022	28.70	6.50	0.000**
	sentence reading (accuracy)	43.90	35.90	0.008	50	34.9	0.004	52.90	48.50	NS	38.30	26.20	0.011
	nonword reading (accuracy)	29.70	22.70	0.011	22.6	7.1	0.001**	48.50	35.50	0.022	19.60	15.00	NS
	word writing	28.50	19.90	0.001**	26.7	23.3	NS	43.50	31.90	0.039	20.00	13.00	NS
	comprehension	11.80	4.60	0.002**	7.7	2.2	NS	14.70	9.30	NS	9.30	0.90	0.004
Memory	personal info	20.80	14.80	0.034	17.8	11.1	NS	35.60	19.20	0.002**	11.20	12.10	NS

	time and space	24.70	13.40	0.000**	20.9	16.5	NS	25.30	13.30	0.049	20.40	11.10	0.041
	immed free recall	25.60	17.20	0.011	28.2	18.8	NS	30.50	22.00	NS	17.50	8.70	0.035
	immed recognition	32.40	26.10	NS	30	31.1	NS	48.70	32.90	0.012	20.60	19.60	NS
	delayed free recall	26.40	24.00	NS	30.6	28.2	NS	36.70	31.70	NS	16.00	17.00	NS
	delayed recognition	27.00	22.60	NS	27.8	24.4	NS	42.30	32.40	NS	14.30	12.40	NS
	task recognition	24.60	13.00	0.000**	25.6	14.6	0.022	30.20	20.60	NS	15.30	5.10	0.021
Number	number reading	23.60	12.30	0.000**	20.9	7	0.000**	33.30	16.70	0.007	15.50	8.70	NS
	number writing	28.40	18.00	0.000**	30.7	19.3	0.041	42.90	24.30	0.000**	18.60	14.70	NS
	calculation	23.30	13.50	0.001**	22.2	13	NS	34.90	18.60	0.016	18.30	10.00	NS
Praxis	multiple object use	22.80	10.50	0.000**	15.7	5.6	0.022	26.00	12.30	0.006	24.50	7.80	0.000**
	gesture production	15.40	11.10	NS	10	5.6	NS	29.30	18.70	NS	2.90	3.80	NS
	gesture recognition	14.70	10.30	NS	12.2	15.6	NS	25.70	17.60	NS	7.70	4.80	NS
	gesture imitation	30.20	16.80	0.000**	29.2	13.5	0.003	38.40	24.70	0.031	25.70	9.50	0.002**
	figure copy	53.00	42.00	0.004	51.8	31.8	0.000**	52.90	41.40	NS	59.00	45.00	0.029

**significant at 0.002 level. [a]McNemar test. Abbreviations: LHD = left brain damaged; RHD = right hemisphere damaged; FU = follow up

Table 4 Multivariate linear regression models for effects of physical, affective and cognitive performance on functional outcomes

-		B	SE	95% CI	p
Model 1					
Outcome = Barthel FU	Barthel	0.36	0.05	0.264 to 0.456	0.000
	Anxiety FU	-0.02	0.07	-0.155 to 0.121	0.806
	Depression FU	-0.17	0.10	-0.364 to 0.022	0.081
	Apathy	-0.05	0.03	-0.108 to 0.017	0.149
	Proportion of tasks impaired	-0.71	0.86	-2.403 to 0.989	0.411
Model 2					
Outcome = NEADL	Barthel	0.50	0.07	0.361 to 0.633	0.000
	Anxiety FU	0.13	0.10	-0.063 to 0.327	0.184
	Depression FU	-0.40	0.14	-0.672 to -0.127	0.004
	Apathy	-0.16	0.05	-0.248 to -0.072	0.000
	Proportion of tasks impaired	-3.47	1.22	-5.866 to -1.067	0.005

Abbreviations: CI = confidence interval; SE = standard error; FU = follow up

Table 5 GLM modelling of domain effects on long term everyday functions, controlling for initial Barthel scores, follow up affect and apathy level

-	Domain		W. Lambda	p	Eta	Power
Multivariate	Spatial Attention		0.920	0.001	0.080	0.917
between subject effects		Barthel FU		NS		
between subject effects		NEADL		0.003	0.072	0.930
Multivariate	Controlled attention		0.959	0.036	0.041	0.631
between subject effects		Barthel FU		NS		
Between subject effects		NEADL		0.035	0.028	0.560
Multivariate	Language		0.978	NS	0.022	0.370
between subject effects		Barthel FU		NS		
between subject effects		NEADL		NS		
Multivariate	Memory		0.984	NS	0.016	0.279
between subject effects		Barthel FU		NS		
between subject effects		NEADL		NS		
Multivariate	Number		0.971	NS	0.029	0.471
between subject effects		Barthel FU		NS		
between subject effects		NEADL		NS		
Multivariate	Praxis		0.919	0.001	0.081	0.922
between subject effects		Barthel FU		NS		
between subject effects		NEADL		0.001	0.063	0.898

Abbreviations: FU = follow up; NEADL = Nottingham Extended ADL scale